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09/996,555	11/15/2001	Gregory Paul Dittmar	8341	2834

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EXAMINER	
FUBARA, BLESSING M	

ART UNIT	PAPER NUMBER
1615	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/996,555	Applicant(s) DITTMAR ET AL.	
	Examiner Blessing M. Fubara	Art Unit 1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *2 & 3* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Examiner acknowledges receipt of IDS filed 04/15/02 and 11/13/02.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 1-24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

3. Claims 1 and 11 are vague and indefinite because it is not clear what a safe and effective amount is. Safe is a relative term since what is safe and effective to one may not be safe and effective to another. Applicants may consider changing part a of claims 1 and 11 to ---a therapeutically active agent---.

4. Regarding claims 3 and 12, the phrase "wax like" renders the claim(s) indefinite because the claim(s) include(s) elements not actually disclosed (those encompassed by "wax like"), thereby rendering the scope of the claim(s) unascertainable. See MPEP § 2173.05(d).

5. Regarding claims 3 and 12, the phrase "such as" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

Regarding claims 3 and 12, applicants may overcome the rejection by deleting the phrase "wax like" and "such as" from claims 3 and 12.

Claims 3 and 12 recite "cellulose derivatives" and further list cellulose ethers, methylcellulose, ethylcellulose, carboxymethylcellulose and carboxymethylethylcellulose, which

are some of cellulose derivatives listed in the claims. The intent of the applicants is not known if the cellulose derivatives include the cellulose derivatives listed in the claims or the cellulose derivatives are outside those recited in the claims. It is suggested that applicants delete "cellulose derivatives" from claims 3 and 12.

6. Claims 23 and 24 recite the limitation "the desired site" in line 1. There is insufficient antecedent basis for this limitation in the claims.

7. Claims 23 and 24 are vague and indefinite because according to the claims, by orally administering the composition of claim 1 or 11, "the desired site of a therapeutically active agent in the gastrointestinal tract" is maintained and it is not clear how the desired site of delivery is maintained and it is unclear what is being claimed. It appears that claims 23 and 24 are methods of orally administering the compositions of claims 1 and 11 to the gastrointestinal tract.

For examination purposes, examiner interprets claims 23 and 24 as methods of orally administering the composition of claim 1 (for claim 23) and claim 11 (for claim 24) to the gastrointestinal tract.

Claim Objections

8. Claims 8, 10, 19 and 21 are objected to because of the following informalities:

Claims 8, 10, 19 and 21 recite 5-ASA without an initial definition for 5-ASA. It is suggested that an initial definition for 5-ASA be recited and 5-ASA placed within parenthesis for subsequent use.

Appropriate correction is required.

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims 1-4, 8-14 and 19-22 rejected under 35 U.S.C. 102(b) as being anticipated by Iamartino et al. (US 5,171,580, cited by applicants on form PTO 1449).

Iamartino discloses an oral pharmaceutical preparation that comprises a core of active ingredient coated with three protective layers (abstract, column 3, lines 15-20). Iamartino states that coating the core of therapeutically active agents with the three layers allows specific and reliable release of the active substance directed to the lower part of the intestine and especially to the large intestine or colon (column 3, lines 8-13). The cores are prepared either by granulation or tableting and the tablets or cores that are coated are included in hard gelatin capsule dosage units (column 5, lines 9, 10, 27-35 and claim 1). Iamartino manufactures tablets using a tablet press (column 5, lines 57-59) and pressing in a tablet press produces compressed tablets. Regarding claim 22, although, Iamartino includes about 10 coated tablets or cores in a capsule (column5, lines 27-55), Iamartino nonetheless teaches the manufacture of tablet by tablet press and thus Iamartino's coated pressed tablet meets the scope of claim 22.

The active agents of Iamartino are 5-aminosalicylic acid (5-ASA) or corticoids for treating colonic and rectal disorders, antibacterial agents and antibiotics for treating local infectious diseases of the large intestine, anti-tumor chemotherapeutic agents for cancer therapy of the large intestine, cimetropium bromide antispasmodic drug, ketoprofen and ibuprofen non

steroidal anti-inflammatory agents, and peptide or protein drugs (column 4, line 35 to column 5 line 2). Iamartino exemplifies the pharmaceutical preparation with ketoprofen (example 1), cimetropium bromide (example 2) and toluidine blue (example 3).

An inner coating layer in Iamartino comprises plasticizer and anionic copolymer EUDRAGIT S where the ratio of free carboxyl group to the ester group is 1:2 and the amount of the copolymer is in the range of 10-30% by weight gain on the core and it is suggested that a film thickness of 40-120 microns would ensure a quick dissolution of the coating layer at above pH 7.0 (column 3, lines 21-23 and lines 36-57).

An intermediate layer of gelling polymer (column 3, lines 24-26) comprises cellulose derivatives (column 3, lines 58-68). An outer layer of gastro-resistant polymer (column 3, lines 28-30) comprises common enteric material that are selected from cellulose acetate phthalate, hydroxypropylmethyl cellulose phthalate, polyvinyl acetate phthalate, hydroxyethyl cellulose phthalate, cellulose acetate tetrahydrophthalate and EUDRAGIT L that dissolves at pH 5.5 (column 4, lines 21-29). The thickness of the outer layer in example 1 of Iamartino is listed as about 30 microns and the purpose of the outer layer is to enable the preparation to quickly dissolve in the intestine (column 3, lines 28-30).

The EUDRAGIT S of Iamartino is the poly(methacrylic acid, methyl methacrylate) 1:2 copolymer recited in instant claims 1-4 and 11-15. EUDRAGIT L is the poly(methacrylic acid, methyl methacrylate) 1:1 copolymer recited in instant claims 1-4 and 11-15. EUDRAGIT L, which is used in the outer layer differs from EUDRAGIT S of the inner layer. Instant claims 1 and 11 is a pharmaceutical composition that comprises a, b and c and the comprises language does not exclude the presence of the intermediate layer in Iamartino.

The teaching of Iamartino meets the limitations of the claims.

11. Claims 1-4, 8, 9, 11-14, 19, 20 and 22 rejected under 35 U.S.C. 102(b) as being anticipated by Rommelmayer (WO 98/27967, provided by applicants on form PTO 1449).

Rommelmayer discloses a compressed tablet formulation for oral administration and the formulation comprises an inner core of biologically active ingredient and excipients, an enteric inner coating layer and an outer coating layer (page 1, lines 3-21 and page 18, lines 31 and 32). Among the biological agents disclosed by Rommelmayer are hydrocortisone, prednisone, diclofenac sodium and piroxicam and ketoprofen and aspirin NSAIDs, codeine, morphine, antibiotics, antimicrobial agents, antihistamines, bronchodilators, antiemetics, antiviral drugs, anti-ulcer drugs, anti-Parkinson drugs, diuretics, calcium antagonists, anti-hypertension drugs, and drugs for treating cardiovascular diseases (page 12, line 17 to page 13 line 7). The inner coating comprises EUDRAGIT L 30D, which is sprayed onto the core (example 1), or phthalate (page 11, lines 4-14). The outer coating comprises EUDRAGIT RL 30D and EUDRAGIT RS 30D, which is also sprayed onto the cores (example 1) and the ratio of the RS and RL determines the release of the active agent (page 11, lines 29 and 30), on page 14, lines 17 and 18, Rommelmayer discloses that the outer coating layer can be either EUDRAGIT RL or a mixture of EUDRAGIT RS and EUDRAGIT RL and on page 11, lines 18-33, Rommelmayer discloses that the outer coating would consist of one or more polymers including EUDRAGIT copolymers. EUDRAGIT L in Rommelmayer is the poly(methacrylic acid, methyl methacrylate) 1:1 copolymer recited in instant claims 1-4 and 11-15. EUDRAGIT RL and EUDRAGIT RS are not the same as EUDRAGIT L (see page 11 of Rommelmayer). The comprising language of

instant claims 1 and 11 does not exclude the presence of excipients and plasticizers. The teachings of Rommelmayer meet the limitations of the claims.

Claim Rejections - 35 USC § 103

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

13. Claim 15 is rejected under 35 U.S.C. 103(a) as being unpatentable over Rommelmayer (WO 98/27967, provided by applicants on form PTO 1449).

Rommelmayer clearly teaches the orally administrable tablet of the instant invention by teaching an oral compressed tablet formulation that comprises a core of active agents, an inner coating layer comprising enteric coating materials selected from hydroxypropylmethylcellulose phthalate, polyvinyl acetate phthalate and acrylic and/or methacrylic acid/ester copolymers and EUDRAGIT L 30D and an outer coating layer comprising erodible polymer film selected from one or more polymers of ethylcellulose, polysiloxan, polyethylene and EUDRAGIT (page 11).

However, Rommelmayer while teaching an outer coating that comprises a mixture of EUDRAGIT RL 30D and EUDRAGIT RS 30D, does not teach an outer coating that is a mixture of poly (methacrylic acid, methyl methacrylate) 1:2 (EUDRAGIT S) and poly (methacrylic acid, methyl methacrylate) 1:1(EUDRAGIT L) as recited in instant claim 15. It would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute a mixture of EUDRAGIT S and EUDRAGIT L for the mixture of EUDRAGIT RL 30D and

EUDRAGIT RS 30D with the expectation that the tablet would release the active agent in the intestines. One having ordinary skill in the art would have been motivated to use the mixed EUDRAGIT co-polymers because Rommelmayer suggests that the use of mixture EUDRAGIT co-polymers in the outer coat layer determines the release of the active agent.

14. Claims 5-7 and 16-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Iamartino et al. (US 5,171,580, cited by applicants on form PTO 1449).

Iamartino clearly teaches the oral formulation of the instant invention by teaching tablets or cores of active agents that are coated by an inner layer comprising EUDRAGIT S (poly(methacrylic acid, methyl methacrylate) 1:2), an intermediate gelling polymer layer and outer layer comprising EUDRAGIT L (poly(methacrylic acid, methyl methacrylate) 1:1) and the tablets are included in a capsule such that the overall dosage form is a capsule (claim 1 and example 1).

Regarding instant claims 7 and 18 that recite the process of making the coated solid dosage form, although Iamartino teaches continuous spray coating of the tablets or cores with the coating layers, it is respectfully submitted that Iamartino teaches coated active cores or tablets and how the coated core is prepared is not critical in a formulation claim.

However, while Iamartino teaches inner layer coating and outer layer coating that has a thickness of from about 40 micron (inner layer) plus 30 micron (outer layer) to about 120 micron (inner layer) plus 30 micron (outer layer), that is, from about 70 micron to about 150 micron, Iamartino does not give the thickness of the coating layers in mg/cm^2. It would have been obvious to one of ordinary skill in the art at the time the invention was made to apply to the cores or tablets an inner and outer coating layer of certain thickness since Iamartino teaches that the

thickness of the coating layers determines the quick dissolution of the coating layer (column 3, lines 48 and 49). One having ordinary skill in the art would have been motivated to optimize the thickness of the coating layer determined either in microns or mg/cm^2 with the expectation of producing desired quick dissolution of the coating layer.

15. Claims 23 and 24 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Rommelmayer (WO 98/27967, provided by applicants on form PTO 1449).

Rommelmayer discloses the orally administrable tablet of the invention because Rommelmayer teaches the coated dosage forms of instant claims 1 and 11 for oral administration. Since the compressed tablet of Rommelmayer is orally administrable and the coating layers determine the release of active agents in the intestines, the teaching of Rommelmayer encompasses the scope of claims 23 and 24. Alternatively, one would be motivated to orally administer the coated tablet of Rommelmayer to the gastrointestinal tract because the method is explicit in Rommelmayer and the coated tablet of Rommelmayer is for oral administration.

16. Claims 23 and 24 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Iamartino et al. (US 5,171,580, cited by applicants on form PTO 1449).

Iamartino discloses the orally administrable formulation of claims 1 and 11 where the coating layer determines the release of active agents in the intestines. Thus the teaching of Iamartino encompasses the scope of claims 23 and 24. In the alternate, the method of administering the formulation of claims 1 and 11 to the gastrointestinal tract is explicit in

Iamartino because the formulation of Iamartino, which anticipates claims 1 and 11 is orally administrable and therefore one would be motivated to orally administer the formulation of Iamartino to the gastrointestinal tract.

17. The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicants' cooperation is respectfully requested in correcting any errors of which applicants may become aware in the specification.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Blessing M. Fubara whose telephone number is 703-308-8374. The examiner can normally be reached on 7 a.m. to 3:30 p.m. (Monday to Friday).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K. Page can be reached on 703-308-2927. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3592 for regular communications and 703-305-3592 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1234.

Blessing Fubara
Patent Examiner
Tech. Center 1600
March 10, 2003